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Obesity: Open Access

Research Article Volume: 1.2 Open Access

Long-term Results of Dyslipidemia after Bariatric Surgery: A Comparison between Gastric Bypass and Sleeve Gastrectomy

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Received date: 03 June 2015; **Accepted date:** 11 August 2015; **Published date:** 17 August 2015.

Citation: Quezada N, Hernández J, León F, Brañes A, Gabrielli M, et al. (2015) Long-term Results of Dyslipidemia After Bariatric Surgery: A Comparison Between Gastric Bypass and Sleeve Gastrectomy. Obes Open Access 1(2): doi http://dx.doi.org/10.16966/2380-5528.104

Abstract

Background: Dyslipidemia is frequent in obese patients. Long-term outcomes of dyslipidemia after bariatric surgery have not been reported. Our aim is to report long-term evolution of dyslipidemia after bariatric surgery, comparing laparoscopic Roux-Y gastric bypass (LRYGB) versus sleeve gastrectomy (LSG).

Methods: Retrospective analysis between 2001 and 2010. Demographics, comorbidities, lipid profiles and excess weight loss (%EWL) at 5 years were retrieved, comparing values and dyslipidemia remission after LRYGB and LSG.

Results: 2.416 LRYGB and 1.408 LSG patients were included. Basal demographics and comorbidities were similar between groups, except for higher body mass index in LRYGB patients. 152 LRYGB and 94 LSG patients achieved 5 years follow-up, reaching 83% and 70% EWL, respectively ($p<0.01$). Long-term dyslipidemia remission for LRYGB and LSG was achieved in 60% and 25% for total cholesterol; 80% and 57% for LDL-cholesterol; 80% and 92% for low HDL-cholesterol and 74% and 59% for triglycerides, respectively. Multivariate analysis showed that total cholesterol and triglycerides were significantly lower in LRYGB patients ($p<0.05$) at the fifth year. LDL-cholesterol and HDL-cholesterol showed no differences between groups ($p=0.08$ and 0.33, respectively).

Conclusion: At long-term, bariatric surgery reach an acceptable remission or improvement of dyslipidemia, especially for total cholesterol and triglycerides after LRYGB compared to LSG.

Keywords: Bariatric surgery; Gastric bypass; Sleeve gastrectomy; Dyslipidemia; Cholesterol; Triglycerides

Introduction

Dyslipidemia is a common feature in obese patients [1] and a major risk factor for the development of atherosclerosis and cardiovascular disease. Dyslipidemias are characterized by elevations in total cholesterol (TC), LDL-cholesterol (LDL-C), low HDL-cholesterol (HDL-C) or elevated triglycerides (Tg) according to NCEP ATP III consensus [2]. Several bariatric surgery (BS) series have reported high prevalence of dyslipidemia in obese patients, reaching values of 40% of hypercholesterolemia and 24% of hypertriglyceridemia [3].

BS has proven to be an effective treatment against obesity-related comorbidities, achieving high rate of remission in diseases such as type 2 diabetes mellitus [4,5] or arterial hypertension [3,6] among others. In the case of dyslipidemia, studies have shown acceptable short-term outcomes after BS, reaching more than 70% of resolution at one year [3]. These results are more pronounced in patients submitted to laparoscopic Roux-y gastric bypass (LRYGB) or bilio-pancreatic diversion (BPD), reaching improvements in the order of 95 to 99% [3]. In the case of laparoscopic sleeve gastrectomy (LSG), it has been reported 85% of resolution of dyslipidemia after the first year after surgery [7,8].

When LRYGB is compared to LSG, LRYGB seems to achieve a better lipid control and dyslipidemia remission at short-term follow-up (at 1 and at 3 years) [9], along with better weight loss control and remission of other comorbidities. In addition, Benaiges et al. [10] in a non-randomized prospective study showed that after one year of follow-up, both procedures induced a decrease in serum lipid levels, although LRYGB was more effective than LSG in controlling TC and LDL-C levels; despite of showing a significant lower HDL-C levels than LSG patients [10].

Currently, there is a lack of data reporting the long-term results of dyslipidemia after BS, especially for Tg, HDL-C and LDL-C. Furthermore, long-term dyslipidemia results after LSG are scarce andeven more, there is scarce data comparing the two most currently performed bariatric procedures (LRYGB and LSG) at the long-term. Therefore, the aim of this study is to report long-term evolution of dyslipidemia after bariatric surgery, comparing LRYGB versus LSG.

Methods

Retrospective analysis of our bariatric surgery database at Pontificia Universidad Católica de Chile was performed, from July 2001 to December 2010. All patients submitted to LRYGB and LSG during this period were included.

Patients were evaluated, educated and followed by a multidisciplinary team in the pre and postoperative period. Demographics, comorbidities, preoperative work-up and surgical results were recorded. Postoperative percentage of excess weight loss (%EWL) and lipids profiles were followed periodically and recorded up to 5 years after surgery. Patients attended the appointments according to their availability and convenience, so follow-up was patient-dependent. When patients did not attend controls, they were contacted via phone calls or emails.

Surgical technique

Patients were submitted to LRYGB or LSG depending on clinical and biochemical criteria. As seen in other series, patients with higher BMI and/or with association of metabolic diseases tend to respond better to LRYGB, while pure and milder obesity is often a better candidate to LSG [9]. Of note, patients with BMI lower than 35 kg/m^2 were also operated, based on BMI's inaccuracy to correctly identify those "metabolically unhealthy people", whose benefits do not only remit to obesity itself but also to their metabolic conditions [11].

LRYGB is performed in our center as described by Higa et al. [12]. Briefly, a stapled entero-enterostomy is performed creating a 150 cm alimentary limb and a 25-30 cm biliopancreatic limb. A small gastric pouch is created and a hand-sewn gastrojejunostomy is performed, antecolic and antegastric, calibrated with a 34F bougie. Petersen´s and mesenteric defects are closed with 2/0 silk.

LSG is performed since 2005 and we calibrate the sleeve with a 50F bougie, firing the first stapler 5 cm proximal to pylorus. The staple line is reinforced with a running absorbable suture.

Metabolic definitions

Dyslipidemia was defined according to NCEP ATP-III guidelines [2]: total cholesterol ≥ 200 mg/dL, LDL-cholesterol ≥ 130 mg/dL (for moderately risk patients), HDL-cholesterol ≤ 40 mg/dL or triglycerides ≥ 150 mg/dL. Remission of dyslipidemia was defined as return to normal values without medication use. Patients taking oral anti-lipemic medications were included in the univariate analysis and excluded from the multivariate analysis at fifth year.

Diagnosis of prior comorbidities was done according to specific criteria: Arterial hypertension was defined by World Health Organization (WHO) criteria; Insulin-resistance was defined according American Association of Clinical Endocrinologists (AACE) criteria and diagnosis of Type 2 Diabetes Mellitus was performed according to criteria established by American Diabetes Association (ADA).

Statistical analysis

Results are expressed as mean ± standard deviation. %EWL and lipids values at different time of follow-up were calculated and compared between both surgical techniques. In addition, a multivariate analysis was performed in order to clarify influence of %EWL in dyslipidemia long-term remission, excluding diabetic patients and patients using anti-lipemic agents. Finally, a subgroup analysis based on preoperative lipid values were normal or altered was performed.

Statistical analysis was performed using t-student for numerical variables with normal distribution and Mann-Whitney test for non-parametric variables. Differences were considered significant when $p<0.05$.

Results

We identified 2.416 patients submitted to LRYGB and 1.408 patients who underwent LSG during this period. Baseline demographics and comorbid conditions were similar between groups, except for higher preoperative body mass index in and use of anti-lipemic agents in the preoperative period in LRYGB patients ($p<0.01$, Table 1).

Follow-up and %EWL evolution of both groups are shown in Figure 1. Complete follow-up was achieved in 326 (27.5%) of LSG and 368 (16.9%) of LRYGB patients at 1 year; 108 (9.1%) of LSG and 193 (8.8%) of LRYGB patients at 3 years; and 94 (7.9%) of LSG and 152 (6.9%) of LRYGB patients at 5 years. Of note, LRYGB achieved significantly higher %EWL since the second postoperative year and this difference persisted over time, reaching 83% and 70% EWL for LRYGB and LSG at 5 years, respectively ($p<0.01$).

	LRYGB (n: 2.416)	LSG (n: 1.408)	p-value
Sex (% of female)*	74%	78%	
Age, years (mean ± SD)*	38 ± 11.2	37 ± 11.7	
BMI, kg/m^2 (mean ± SD)	39.8 ± 5.2	35.3 ± 3.9	<0.0001
Type 2 diabetes mellitus, %*	5.5%	4.9%	
Insulin-resistance, %*	55%	52%	
Arterial hypertension, %*	28%	24%	
Any dyslipidemia, %* Anti-lipemic treatment %**	56% 31%	53% 20%	<0.0001

Table 1: Baseline demographics and comorbid conditions of LRYGB and LSG patients

*p>0.05

Abbreviations: LRYGB: laparoscopic Roux-y gastric bypass; LSG: laparoscopic sleeve gastrectomy, SD: standard deviation; BMI: body mass index.

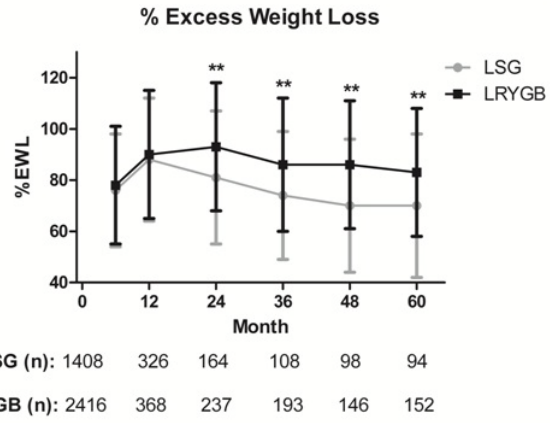

Figure 1: Follow-up (n) and excess weight loss evolution of LSG and LRYGB patients

Abreviations: %EWL: percentage of excess weight loss; LSG: laparoscopic sleeve gastrectomy, LRYGB: Laparoscopic Roux-y gastric bypass.

*** p<0.01.*

Total cholesterol evolution

Preoperative TC levels were similar between groups. Since the third postoperative month, LRYGB achieved lower TC levels than LSG patients, and this effect was sustained over time up to the fifth postoperative year, reaching a significant difference (Figures 2a).

In regard to preoperative hypercholesterolemia, 49% of LRYGB and 48% of LSG patients had high preoperative TC levels (or taking oral medications). This percentage decreased to 7% and 33% respectively at sixth postoperative month and then increased slowly over time, reaching 33% in LRYGB and 51% in LSG at fifth year (Figure 2b).

When considering only patients with normal preoperative TC (and no oral medication), 45% of LSG and 16% of LRYGB patients developed high TC at five years follow-up (Figure 2c). In the other hand, when considering only patients with elevated preoperative TC (or taking oral medications), 75% of LSG and 40% of LRYGB patients persisted with elevated TC at fifth year, thus achieving 25% and 60% of hypercholesterolemia long-term remission respectively (Figure 2d).

LDL-cholesterol evolution

In the same way of TC, LRYGB patients showed significant lower

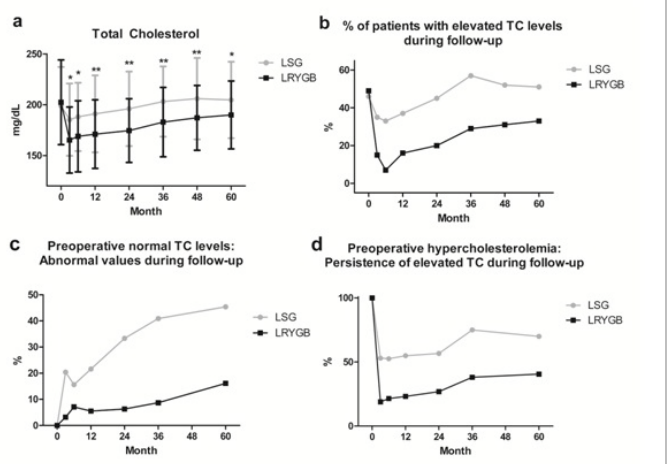

Figure 2: Total cholesterol evolution during follow-up. a) TC values evolution. b) Percentage of patients with abnormal TC values (or taking anti-lipemic oral medications) during follow-up. c) Percentage of patients with normal preoperative TC who developed abnormal TC values during follow-up. d) Percentage of preoperative hypercholesterolemic patients that persisted with high TC values during follow-up.

Abreviations: TC: total cholesterol; LSG: laparoscopic sleeve gastrectomy; LRYGB, Laparoscopic Roux-y gastric bypass.

**p<0.01*

***p<0.001.*

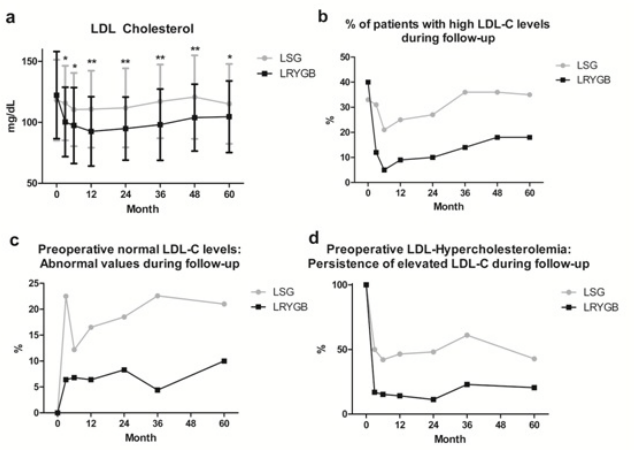

Figure 3: LDL-cholesterol evolution during follow-up. a) LDL-C values evolution. b) Percentage of patients with abnormal preoperative LDL-C values (or taking oral medications) during follow-up. c) Percentage of patients with normal preoperative LDL-C who developed abnormal values during follow-up. d) Percentage of preoperative LDL-hypercholesterolemic patients that persisted with high LDL-C values during follow-up.

Abreviations: LDL-C: LDL-cholesterol; LSG: laparoscopic sleeve gastrectomy; LRYGB: Laparoscopic Roux-y gastric bypass.

**p<0.01*

***p<0.001*

LDL-C levels than LSG patients as soon as the third postoperative month and it was sustained over time (Figure 3a).

In the preoperative period, 40% of LRYGB and 35% of LSG patients showed high LDL-C levels, respectively. Six months after surgery, 20% of LSG patients had high LDL-C levels and thereafter there was a rise up to 38% at the fifth year post op. In the other hand, 4.5% of LRYGB patients had high LDL-C levels six months after surgery and there was an increase to 19% at the fifth year (Figure 3b).

In patients who had normal preoperative LDL-C levels, 21% of LSG and 10% of LRYGB patients developed elevated LDL-C at 5 years follow-up (Figure 3c). Finally, 43% of LSG and 20% of LRYGB patients who had preoperative high levels of LDL-C persisted with abnormal values after surgery, thus achieving 57% and 80% of LDL-hypercholesterolemia long-term remission, respectively (Figure 3d).

HDL-cholesterol evolution

Patients in the LSG group showed significant higher levels after the third and sixth postoperative months compared to LRYGB. Nevertheless, one year after surgery, there were no differences between both groups and it was sustained over time (Figure 4a).

There were no differences in percentage of patients with abnormal values between groups at long-term follow-up (p=0.09), except for the first six months after surgery when LRYGB patients showed a higher percentage of abnormal HDL-C levels (Figure 4b).

In patients with normal preoperative HDL-C levels (Figure 4c), both procedures showed minimal differences during follow-up and only 4% of patients developed abnormal HDL-C after five years. In the other hand, in patients with low preoperative HDL-C levels, 7.7% and 20% of LSG and LRYGB patients persisted with low HDL-C levels at 5 years follow-up, thus achieving 92% and 80% of HDL-hypocholesterolemia long-term remission, respectively (Figure 4d).

Triglycerides evolution

LRYGB patients showed significant higher Tg levels before surgery. Both groups decreased Tg levels after surgery; nevertheless since the first year and up to the fifth year, LRYGB achieved significant lower Tg levels than LSG patients (Figure 5a).

In the preoperative period, 49% and 42% of LRYGB and LSG patients had hypertriglyceridemia, respectively. Both procedures produced a drop in those percentages, reaching the lowest percentage at the sixth postoperative month in the LSG group (17%) and in the 12th month in the LRYGB group (8.6%). Thereafter, there was a rise in the percentage of high Tg levels over time, reaching 28% and 17% in the LSG and LRYGB patients at 5 years, respectively (Figure 5b).

After 5 years, 21% of LSG patients who had normal preoperative Tg developed hypertriglyceridemia and this phenomenon occurred only in 2.5% of LRYGB patients (Figure 5c). On the other hand, 41% of LSG and 26% of preoperative hypertriglyceridemic LRYGB patients persisted with high Tg levels at fifth year, thus achieving 59% and 74% of hypertriglyceridemia long-term remission, respectively (Figure 5d).

Multivariate analysis

Multivariate analysis of lipid values at fifth year, adjusted by %EWL, showed that TC and Tg values were significantly lower in LRYGB patients (p=0.006 and p=0.017 respectively) compared to LSG patients. HDL-C and LDL-C levels showed no differences between groups (p=0.335 and p=0.086 respectively, Table 2). As we mentioned before, diabetic patients (3 patients in each group at 5 years) and patients on anti-lipemic treatment (19 LRYGB patients and 9 LSG patients) were excluded from 5-year multivariate analysis.

Discussion

Dyslipidemias are a major risk factor for cardiovascular disease, the main cause of mortality worldwide. Obesity is frequently associated with

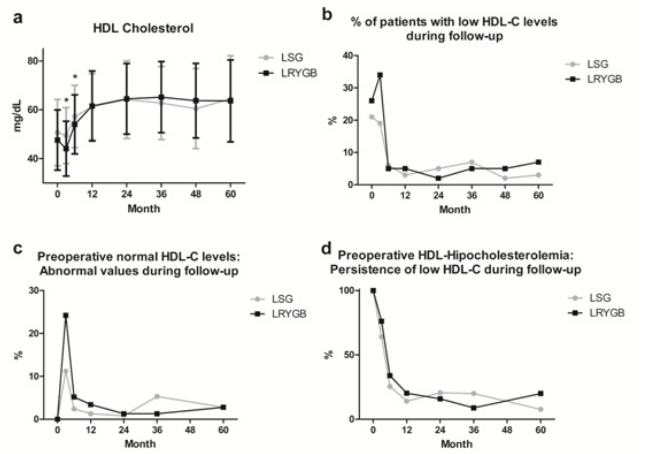

Figure 4: HDL-cholesterol evolution. a) HDL-C values during follow-up. b) Percentage of patients who had low HDL-C during follow-up. c) Percentage of patients who had preoperative normal HDL-C and developed low HDL-C levels during follow-up. d) Percentage of preoperative HDL-hypocholesterolemic patients that persisted with low HDL-C values during follow-up.

Abreviations: HDL-C: HDL-cholesterol; LSG: laparoscopic sleeve gastrectomy; LRYGB: Laparoscopic Roux-y gastric bypass.

**p<0.05.*

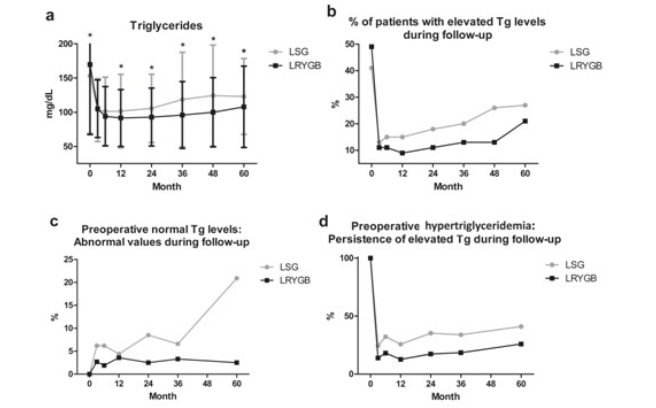

Figure 5: Triglycerides evolution during follow-up.a) Tg values during follow-up. b) Percentage of patients with abnormal Tg levels during follow-up. c) Percentage of patients with preoperative normal Tg levels and developed high Tg levels during follow-up. d) Percentage of preoperative hypertriglyceridemic patients that persisted with high Tg levels during follow-up.

Abreviations: Tg: Triglycerides; LSG: laparoscopic sleeve gastrectomy; LRYGB: Laparoscopic Roux-y gastric bypass.

**p<0.05.*

dyslipidemia [1] and BS is the most effective treatment for obesity [13], with a high rate of prevention [14] and remission of comorbid conditions after surgery, including dyslipidemia [3,4,13,15]. Recently, a meta-analysis by Gloy et al. [16] showed that BS produced better control of LDL-C, HDL-C and Tg than non-surgical treatment, but studies included in this analysis were limited to a maximum of two years of follow-up.

Among the different types of bariatric surgeries, BPD and LRYGB

	LRYGB	LSG	Univariate analysis (LRYGB vs LSG) p	Multivariate analysis (adjusted by %EWL) p*
TC value (mean ± SD)	190 ± 33 mg/dL	204 ± 37 mg/dL	0.001	0.006
TG value (mean ± SD)	107 ± 59 mg/dL	123 ± 55 mg/dL	0.009	0.017
HDL-C value (mean ± SD)	63 ± 16 mg/dL	64 ± 17 mg/dL	0.91	0.335
LDL-C value (mean ± SD)	104 ± 29 mg/dL	115 ± 32 mg/dL	0.01	0.086

Table 2: Uni and multivariate analysis of lipid values at fifth year, LRYGB vs LSG

*Diabetic patients and patients on anti-lipemic treatment were excluded from multivariate analysis.

Abbreviations: LRYGB: Laparoscopic Roux-Y Gastric Bypass; LSG: Laparoscopic Sleeve Gastrectomy; %EWL: Percentage of excess weight loss; TC: Total cholesterol; TG: Triglycerides; HDL-C: HDL-cholesterol; LDL-C: LDL-cholesterol; SD: standard deviation

have shown good results in terms of remission of dyslipidemia [3,17], but at least for LSG there is still scarce information. It has been published that LSG can achieve dyslipidemia remission equally to LRYGB but this reports have evaluated their results only up to one-year after surgery. Also, it has been proposed that both techniques have comparable good results in terms of control of cardiovascular risk factors. Nevertheless, these results are again only one-year post op and therefore no real conclusions can be made upon this information [18,19].

In the case of mid or long-term outcomes, few series have demonstrated good results in improvement of dyslipidemia and mainly they have assessed LRYGB. Courcoulas et al. [20] showed that after 3 years of follow-up, LRYGB produced a 61.9% of dyslipidemia remission, although their cut-off points to define dyslipidemia were higher compared to other series. In the Utah obesity study [21], LRYGB showed at sixth postoperative year a resolution of high LDL-C, low HDL-C and high Tg levels of 53%, 67% and 71% respectively.

Our results showed that RYGB achieved higher dyslipidemias remission than LSG, particularly in TC and Tg levels with no major differences in HDL-C and LDL-C levels on multivariate analysis at the fifth year. Recently, Ruiz-Tovar et al. [22] reported that LSG induces favorable changes in Tg and HDL-C levels, but when surgery is coupled with exercise, it can also induces favorable changes in TC and LDL-C levels [22]. Nevertheless, these results were evaluated one year after surgery and it is also known that most patients do not follow regular exercise after surgery.

The pathophysiological mechanism underlying dyslipidemia remission after LRYGB or LSG are not fully studied yet and many hypotheses have been proposed. For example, it has been demonstrated that derivative surgeries such as BPD or LRYGB, induce a decrease in cholesterol absorption [23,24] and probably the length of the alimentary limb (or the length of intestine excluded from bilio-pancreatic secretions) can affect the rate of absorption, since LRYGB and BPD patients reduce cholesterol absorption in 30% and 50% respectively [23,24].

There are other mechanisms, not explored so far, that can explain dyslipidemia improvement or remission after BS, such as the changes in bile acid kinetics. For example, it has been proposed that higher turnover of bile salts as well as higher plasmatic levels of bile acids after LRYGB [25-27] could produce a decrease in hepatic secretion of VLDL particles by reducing the expression of the microsomal transfer protein, a key enzyme involved in VLDL secretion [28]. This mechanism is also valid for the reduction of triglycerides levels since bile acids in the liver can decrease

the expression of the key master factor involved in fatty acid synthesis (SREBP1c) [29].

Regarding to HDL-C levels after BS, it has been proposed that fluctuations can be explained by the "mirror image" of triglycerides reduction, since both particles have a cross-talk in plasma through the cholesteryl-ester transfer protein which passes phospholipids and cholesterol from VLDL to HDL, making the HDL particle more dense and liable to degradation and thus reducing the number of particles as well as the levels of HDL-C. Therefore, reducing plasmatic triglycerides should diminish this inter-particle cross-talk and then HDL-C should increase. In our study, HDL-C levels were higher during the first year in the LSG group and then no differences were observed compared to LRYGB. These results are not explained only by the Tg reduction achieved, since LRYGB patients reached a significant reduction of Tg levels compared to LSG. These facts suggest that the pathophysiological mechanism of HDL-C metabolism is beyond the plasmatic cross-talk between Tg and HDL particles. Finally, it is important to note that hepatic and peripheral enzymes involved in LDL-C, HDL-C and triglycerides metabolism have not been studied yet.

Besides the speculative pathophysiological mechanism underlying the changes in lipid homeostasis, our study has shown a consistent good long-term profile of dyslipidemia evolution after BS, especially after LRYGB. Nevertheless, this study has several limitations, among which the most important is that it is a retrospective analysis with a very small long-term follow-up for both groups. As described in Methods, follow-up was made with clinical controls and laboratory tests, to which patients attended according to their convenience. Although in many cases patients were reached via phone calls, it is observed that a large proportion did not come to controls, possibly due to the initial results of surgery, which is often seen in bariatric series. Even so, the absolute number of followed patients still accounts for a considerable five-year dyslipidemia follow-up, with more than a hundred patients at almost each assessment point. Furthermore, in this context, it has to be noted that lipid profile measurements at different points had a high correspondence in each patient. Therefore it is possible that our good results can be explained since patients followed were more rigorous in following post-operative indications, including diet and exercise. In addition, diet composition during the postoperative period was not standard between patients and it was variable over time; therefore our results can be influenced by nutritional intake besides type of bariatric surgery performed, anti-lipemic treatment or %EWL achieved.

In conclusion, this series showed that BS achieves an acceptable remission or improvement of dyslipidemia at long-term follow-up, especially for LRYGB compared to LSG patients in terms of TC and Tg.

Conflicts of Interest Disclosure Statement

Drs. Nicolás Quezada, Felipe León, Julián Hernández, Alejandro Brañes, Mauricio Gabrielli, Gustavo Pérez, Fernando Pimentel and Alejandro Raddatz has no conflicts of interest or financialties to disclose.

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